

### EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to Applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Pehr Jansson on June 4, 2010.

The application has been amended as follows:

In **Claim 13**, line 4, after "porous" - - raw - - has been inserted.

In **Claim 13**, line 4, after "size" - - predominantly - - has been inserted.

In **Claim 16**, line 4, after "porous" - - raw - - has been inserted.

In **Claim 16**, line 4, after "size" - - predominantly - - has been inserted.

In **Claim 19**, line 4, after "porous" - - raw - - has been inserted.

In **Claim 19**, line 4, after "size" - - predominantly - - has been inserted.

In **Claim 19**, line 6, "flash chromatography tube" has been deleted and - - low-pressure glass tube or syringe body - - has been substituted therefor.

In **Claim 20**, line 1, "The method of purifying a product of Claim 19" has been deleted and - - The pre-filled flash chromatography column according to Claim 19- - has been substituted therefor.

In **Claim 22**, line 4, after "porous" - - raw - - has been inserted.

In **Claim 22**, line 4, after "size" - - predominantly - - has been inserted.

In **Claim 22**, line 6, "flash chromatography tube" has been deleted and - - low-pressure glass tube or syringe body - - has been substituted therefor.

In **Claim 23**, line 1, "The method of purifying a product of Claim 22" has been deleted and - - The pre-filled flash chromatography column according to Claim 22- - has been substituted therefor.

### REASONS FOR ALLOWANCE

2. The following is an examiner's statement of reasons for allowance: **Claims 7-24** are allowable over the prior art of record in view of the claim amendments made herein and for the reasons enumerated in Applicant's response filed May 2, 2010, and the 37 C.F.R. 1.132 Declaration filed May 2, 2010.

3. No new matter is introduced by the recitation of "plastic" or "low-pressure glass" in **Claims 13, 16, 19 and 22** as "a person of ordinary skill in the art would typically employ a glass or plastic tube or syringe body to construct a flash chromatography column" (Applicant's Response, 5/2/2010, p. 7; 37 C.F.R. 1.132 Declaration filed May 2, 2010, p. 2-3 and Exhibits A-D). See *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

4. Williams (US 5,559,039) discloses a column for liquid chromatography comprising spherical and porous silica gel having a particle size of 4.5 micrometers and a pore size of 60 angstroms (Williams, "Abstract;" c. 7, l. 22-39; c. 8, l. 46-48; "Example 1"). However, Williams utilizes coated bonded silica (Applicant's Response, 5/2/2010, p. 11-12) as opposed to raw silica, as required by **Claims 13, 16, 19 and 22**, as

Art Unit: 1793

amended herein. There is no teaching, disclosure, or suggestion in Williams to modify the coated bonded silica with raw silica. Nor would there be any motivation from the prior art to do so.

5. Koh (*Journal of Chromatography*) discloses a column for preparative liquid chromatography comprising spherical and porous silica gel having a particle size of 6 micrometers and a pore size of 60 angstroms (Koh, "Abstract;" p. 225, "Table 1"). Koh further discloses a column for preparative liquid chromatography comprising spherical and porous silica gel having a particle size of 12 micrometers and a pore size of 90 angstroms (Koh, "Abstract;" p. 225, "Table 1"). However, Koh utilizes a stain-less steel chromatography column (Applicant's Response, 5/2/2010, p. 12-13) as opposed to a plastic or low-pressure glass flash chromatography column, as required by the instant invention. Amended **Claims 13 and 16** require a plastic tube or syringe body, and amended **Claims 19 and 22** require a low-pressure glass tube or syringe body. HPLC columns "would not be constructed from plastic or glass tubes or syringes as such materials do not withstand the high pressures used in HPLC" (37 C.F.R. 1.132 Declaration filed May 2, 2010, p. 2, 2<sup>nd</sup> bullet point). The column of Koh is constructed of stain-less steel (Applicant's Response, 5/2/2010, p. 12). There is no teaching, disclosure, or suggestion in Koh to modify the stain-less column with plastic or low-pressure glass. Nor would there be any motivation from the prior art to do so. Further, Koh utilizes chemical bonded octadecyl silica (Applicant's Response, 5/2/2010, p. 12-13) as opposed to raw silica, as required by **Claims 13, 16, 19 and 22**, as amended herein. There is no teaching, disclosure, or suggestion in Koh to modify the chemical

Art Unit: 1793

bonded octadecyl silica with raw silica. Nor would there be any motivation from the prior art to do so.

6. SUPELCO (*Guide to Solid Phase Extraction*) discloses a column for preparative liquid chromatography comprising porous silica gel having a particle size of 40 micrometers and a pore size of 60 angstroms (SUPELCO, p. 1-3, 5-8, 10 and 11). However, SUPELCO discloses a solid phase extraction column that uses irregular shaped raw silica, as opposed to the spherical or semi-spherical shaped silica as required by the instant invention (Applicant's Response, 5/2/2010, p. 13; 37 C.F.R. 1.132 Declaration filed May 2, 2010, p. 3-4). There is no teaching, disclosure, or suggestion in SUPELCO to modify the irregular shaped raw silica with spherical or semi-spherical raw silica. Nor would there be any motivation from the prior art to do so.

7. Schwartz (US 5,128,114) discloses a column for chromatography comprising spherical and porous silica gel having a particle size of 5-20 micrometers and a pore size of 2-20 nanometers (Schwartz, "Abstract;" c. 1, l. 12-18 and 53-56; c. 3, l. 9-12 and 45-49; c. 5, l. 29-33; c. 8, l. 62-64; c. 9, l. 47-51). However, Schwartz does not specify which type of chromatography column is used, and at the time of Schwartz, materials like that of Schwartz were used in HPLC columns (Applicant's Response, 5/2/2010, p. 13-14). Silence is not sufficient to infer that the chromatography column of Schwartz would be a flash chromatography column. There is no teaching, disclosure, or suggestion in Schwartz to modify the chromatography column with a plastic or low-pressure glass flash chromatography column. Nor would there be any motivation from the prior art to do so.

Art Unit: 1793

8. Kanda (US 6,360,589 B1) discloses a column for preparative liquid chromatography comprising spherical and porous silica gel having a particle size of 3-50 micrometers and a pore size of 60-80 angstroms (Kanda, "Abstract;" Figures 1-4; c. 1, l. 5-10; c. 11, l. 16-35; c. 14, l. 9-11). However, Kanda utilizes silicone polymer-coated silica (Applicant's Response, 5/2/2010, p. 14-15) as opposed to raw silica, as required by **Claims 13, 16, 19 and 22**, as amended herein. There is no teaching, disclosure, or suggestion in Kanda to modify the silicone polymer-coated silica with raw silica. Nor would there be any motivation from the prior art to do so.

9. Teraoka et al. (US 5,587,082) discloses a column for preparative chromatography comprising porous silica gel having a particle size of 37 micrometers and a pore size of 15 nanometers (Teraoka, "Abstract;" Figure 1; Examples). However, Teraoka utilizes irregular shaped silated silica (Applicant's Response, 5/2/2010, p. 15-16 and Exhibit A) as opposed to spherical or semi-spherical raw silica, as required by **Claims 13, 16, 19 and 22**, as amended herein. There is no teaching, disclosure, or suggestion in Teraoka to modify the irregular shaped silated silica with spherical or semi-spherical raw silica. Nor would there be any motivation from the prior art to do so.

10. Matsushita et al. (US 4,341,634) discloses a column for chromatography comprising spherical and porous silica gel having a particle size of 4-40 micrometers and a pore size of 80-100 angstroms (Matsushita, "Abstract;" c. 2, l. 41-50). However, Matsushita utilizes a stain-less steel HPLC column (Applicant's Response, 5/2/2010, p. 16 and Exhibit B) as opposed to a plastic or low-pressure glass flash chromatography column, as required by the instant invention. Amended **Claims 13 and 16** require a

Art Unit: 1793

plastic tube or syringe body, and amended **Claims 19 and 22** require a low-pressure glass tube or syringe body. HPLC columns "would not be constructed from plastic or glass tubes or syringes as such materials do not withstand the high pressures used in HPLC" (37 C.F.R. 1.132 Declaration filed May 2, 2010, p. 2, 2<sup>nd</sup> bullet point). There is no teaching, disclosure, or suggestion in Matsushita to modify the stain-less HPLC column with a plastic or low-pressure glass flash chromatography column. Nor would there be any motivation from the prior art to do so.

11. Watanabe et al. (*Journal of Bacteriology*) discloses a column for chromatography comprising 200/350 mesh spherical silica gel (Watanabe, p. 2293). While Watanabe does not explicitly disclose the silica gel having pores with a size between 30 and 300 angstroms, the silica gel disclosed by Watanabe (Fuji-Davidson's microbead silica gel 4B, 200/350 mesh) has an average pore size of 7.7 nm, as evidenced by Kamegawa (*Journal of Colloid and Interface Science*) (Kamegawa, p. 94, "Materials"). However, the 200/350 mesh spherical silica gel of Watanabe contains particles in the range from 42 microns to 74 microns (200 mesh is 74 microns and 350 mesh is 42 microns) (Applicant's Response, 5/2/2010, p. 16-17). "Thus, the range of particles in Watanabe's stationary phase include many particles well outside of the claimed range of 3 to 45 [microns]" (Applicant's Response, 5/2/2010, p. 17). As amended herein, **Claims 13, 16, 19 and 22** require the silica gel to have a particle size "predominantly" between 3 and 45 microns. There is no teaching, disclosure, or suggestion in Watanabe or Kamegawa to modify the 42-74 micron size range of the silica gel with a size range predominantly

between 3 and 45 microns. Nor would there be any motivation from the prior art to do so.

12. Danishefsky et al. (US 2002/0058817 A1) discloses a column for flash chromatography comprising silica gel with a particle size between 40 and 63 micrometers (Danishefsky, 0394). While Danishefsky does not explicitly disclose the silica gel having pores with a size between 30 and 300 angstroms, the silica gel disclosed by Danishefsky has an average pore size of 80 angstroms, as evidenced by Sigma-Aldrich (Sigma-Aldrich, "Silica gel"). However, the closest Sigma-Aldrich silica material (Sigma-Aldrich S6628) is irregular shaped silica (Applicant's Response, 5/2/2010, p. 17-19 and Exhibits C and D). There is no teaching, disclosure, or suggestion in Danishefsky or Sigma-Aldrich to modify the irregular shaped silica with spherical or semi-spherical silica. Nor would there be any motivation from the prior art to do so.

13. Still et al. (*J. Org. Chem.*) discloses a column for flash chromatography comprising silica gel with a particle size between 40 and 63 micrometers (Still, p. 2923-2924). While Still does not explicitly disclose the silica gel having pores with a size between 30 and 300 angstroms, the silica gel disclosed by Still has an average pore size of 80 angstroms, as evidenced by Sigma-Aldrich (Sigma-Aldrich, "Silica gel"). However, the closest Sigma-Aldrich silica material (Sigma-Aldrich, 227196 Silica Gel) is irregular shaped silica (Applicant's Response, 5/2/2010, p. 19-20 and Exhibits E and F). There is no teaching, disclosure, or suggestion in Still or Sigma-Aldrich to modify the

Art Unit: 1793

irregular shaped silica with spherical or semi-spherical silica. Nor would there be any motivation from the prior art to do so.

14. New method claims, **Claims 7-12**, are allowable over the prior art of record because none of the cited references disclose a method for purifying a product comprising performing flash chromatography with a flash chromatography column pre-filled with spherical/semi-spherical and porous silica gel having a particle size between 3 and 45 microns and pores between 30 and 300 angstroms. Still et al. (*J. Org. Chem.*) discloses a method for purifying a product comprising performing flash chromatography by introducing an eluent with at least one product to be purified into a flash chromatography column pre-filled with silica gel with a particle size between 40 and 63 micrometers, causing the eluent to flow through the pre-filled column, and obtaining a separation of the at least one product to be purified (Still, p. 2923-2925). While Still does not explicitly disclose the silica gel having pores with a size between 30 and 300 angstroms, the silica gel disclosed by Still has an average pore size of 80 angstroms, as evidenced by Sigma-Aldrich (Sigma-Aldrich, "Silica gel"). However, the closest Sigma-Aldrich silica material (Sigma-Aldrich, 227196 Silica Gel) is irregular shaped silica (Applicant's Response, 5/2/2010, p. 19-20 and Exhibits E and F). There is no teaching, disclosure, or suggestion in Still or Sigma-Aldrich to modify the irregular shaped silica with spherical or semi-spherical silica. Nor would there be any motivation from the prior art to do so.

15. Any comments considered necessary by Applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably



Art Unit: 1793

accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRITTANY M. MARTINEZ whose telephone number is (571) 270-3586. The examiner can normally be reached on Monday-Friday 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stanley Silverman can be reached on (571) 272-1358. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wayne Langel/  
Primary Examiner, Art Unit 1793

Application/Control Number: 10/536,853

Page 11

Art Unit: 1793

BMM

/Brittany M Martinez/

Examiner, Art Unit 1793